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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,468	07/24/2000	Lee Arnold	BBI-6049	4509

959 7590 03/14/2003

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BOSTON, MA 02109

EXAMINER
KIFLE, BRUCK

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/621,468	Arnold et al.
Examiner	**Art Unit**
Bruck Kifle, Ph.D.	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 10, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *18-21 and 23-45* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *18-21 and 23-45* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's amendments and remarks filed 2/10/03 have been received and reviewed. Claims 18-21 and 23-45 are pending in this application.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 18 is again rejected under 35 U.S.C. 102(b) as being anticipated by Hiremath et al. (Indian J. Chem., Sect. B (1988), 27B(8), 758-62). The claim reads on compounds 8a-f and 13a-d on page 761.

Claim 18 is again rejected under 35 U.S.C. 102(b) as being anticipated by Mitra et al. (Acta Cienc. Indica, Chem. (1985), 11(4), 267-72). The reference teaches the compound with RN 68761-49-9 which corresponds to the compound of the instant claim when in the instant case R^1 is methyl and R is phenyl.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al. (US 6,107,487). The reference teaches the compound of example 10 (see cols 13-14). The claim differs by having a hydrogen over the prior art methyl on the ring nitrogen of the pyrazolinone.

Tertiary versus secondary amines are homologues. Mono-substituted piperazines were found unpatentable over disubstituted piperazines in Ex Parte Weston and Hamlin 121 USPQ 428. It was stated "... any chemist is readily aware of the difference between secondary and tertiary amines, including their reactivities, particularly with respect to the possibility of further substitution for the H in the secondary amine." Ex parte Bluestone, 135 USPQ 199, and In re Doebel, 179 USPQ 158 further affirm that N-CH_3 is obvious over N-H. In re Hoeksema, 154 USPQ 169 in stating that secondary and primary amines are homologues state "...a chemist looking at the formula for another compound which differs so slightly that it is called a homolog generally expects the second compound to have properties similar to the first one.".

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mitra et al. (Acta Cienc. Indica, Chem. (1985), 11(4), 267-72). The reference teaches compounds embraced by the generic claim 1 which Applicants have now excluded by proviso. However, compound that are analogues, homologues or ring position isomers of these prior art compounds are embraced by the claim and render the claim obvious.

For example;

A compound wherein R^1 is methyl and R is 2-hydroxy-3-chlorophenyl embraced by the claim is rendered obvious by the prior art compound wherein R^1 is methyl and R is 2-hydroxy-3-bromophenyl (one halogen renders the other obvious)

A compound wherein R^1 is methyl and R is 4-hydroxy-3-bromophenyl embraced by the claim is rendered obvious by the prior art compound wherein R^1 is methyl and R is 2-hydroxy-3-bromophenyl (ring position isomer).

A compound wherein R^1 is ethyl and R is 2-hydroxy-3-bromophenyl embraced by the claim is rendered obvious by the prior art compound wherein R^1 is methyl and R is 2-hydroxy-3-bromophenyl (methyl versus ethyl).

Claim Rejections - 35 USC § 112

Claim 18-21 and 23-45 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

iii) Regarding the term "substituted" without saying which substituents are intended, Applicants point to page 12, lines 12-25 of the specification. However, this definition is insufficient because it is open-ended and/or is limited to mere examples. Should Applicants intend only these examples, then these should be included within the claims. Applicants are reminded that although the claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., In re Van Guens, 988 F.2d 1181, 26

PSPG2d 1057 (Ded. Cir. 1991)). Accordingly, without the recitation of all these critical limitations, the claims do not adequately define the instant invention.

iv) Regarding claims 28-36, Applicants argue that the protein kinases are from 1 and/or two classes and point to page 91, lines 16-24. The claims need to be limited to these because the claim as presented is broader than the broadest description in the specification. Applicants, however, were unable to say who needs inhibition (does everybody need inhibition) or what the utility is of the in vitro method. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference.

v) Regarding claim 29, Applicants were unable to say who needs to have one or more protein kinases inhibited.

Claims 28-38 are again rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants arguments have been fully considered but is not persuasive. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference. In this art, no compound has yet shown clinical efficacy against every type of cancer. To quote Salmon (Principles of Cancer Therapy) in the paragraph on page 1038 titled Medical Therapy "Curative therapy has been developed for a series of relatively uncommon neoplasms and useful palliative therapy has been developed for some common forms of cancer (Table 162-

4). With rare exceptions, effective therapy has utilized combinations of anticancer drugs." Applicant's attention is drawn to Tables 162-6, 162-7, 162-8, 162-162-9, 162-10, and the material on pages 1045-1046 titled Miscellaneous Anticancer Agents in Salmon (Principles of Cancer Therapy). Different agents are used for different specific forms of cancer and no single agent is listed as a treatment of every single type of cancer. No compound has shown clinical efficacy against all cancers, thus no *in vivo* or *in vitro* assay could be validated for the identification of such a general agent. Applicants' specification logically must lack such assay data.

Regarding the method of claims 28-36, where it was deemed that these claims would read on inhibiting one or more protein kinase activities *in vitro*, inhibiting one or more protein kinase activities in mammals with below normal protein kinase activities, inhibiting one or more protein kinase activities in mammals with normal protein kinase activities, or in asymptomatic mammals with up-regulated protein kinase activities. The specification, however, fails to teach any benefit to be gained from such actions. Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' inhibitor falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision

of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

Applicants have not responded to this.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Provisos have been included in these claims that (i) excludes a compound and (ii) reads "provided that when R^1 is methyl, R is not hydroxymethyl, nitrophenyl, m-$OCH_3C_6H_4$, 4-hydroxy-3-methoxyphenyl or 2-hydroxy-3-bromophenyl." These provisoes lack description. Even negative limitations require a description. The MPEP at 2173.05(i) Negative Limitations states "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984)" and, further, "Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing

to comply with the written description requirement." In the instant case, the new concept that has been introduced by the proviso is the specific relationships between the variables R^1 and R. This specific relationship of connectivity was previously not disclosed. This notion that the definition of one variable depends on the definitions of other variables is new. The definition of a variable is no longer independent.

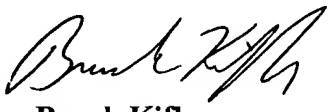
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is (703) 305-4484.

The fax phone number for this Group is (703) 308-4556 or (703) 305-3592. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

March 13, 2003



Bruck Kifle
Primary Examiner
Art Unit 1624